

THE USE OF A RESPIRATORY BIOFEEDBACK DEVICE TO REDUCE DENTAL ANXIETY IN CHILDREN: A RANDOMIZED CONTROLLED CLINICAL TRIAL

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ABSTRACT

INTRODUCTION: Dental anxiety occurs when the patient presents to the dentist with the anticipation of dental treatment. Many children react to dental stressful situations through uncooperative behaviors.

OBJECTIVES: Investigate the effect of a respiratory biofeedback device (RESPeRATE™) in reduction of preoperative anxiety in children undergoing dental procedures under local anesthesia.

MATERIALS AND METHODS: A randomized controlled clinical trial comprising 110 healthy children, of age range 7-12 years, were selected. Their scores were 19 or more according to the Faces version of Modified Child Dental Anxiety Scale. Participants were randomly allocated into two groups: Study and Control group.

For both groups, heart rate was recorded prior to local anesthesia administration and a salivary sample was collected to measure the salivary amylase.

The study group was submitted to a session of respiratory biofeedback "RESPeRATE™". The control group was managed by a routine behavioral management technique "Tell, Show and Do".

Infiltration or block local anesthesia injections were administered, after which heart rate measurement and salivary sample was repeated. T and paired T tests were used for statistical analysis.

RESULTS: Heart rate decreased significantly in the study group (P=0.001), and increased significantly in the control group (P=0.002). There were non-significant changes among both groups regarding salivary amylase. A weak correlation was found between heart rate and salivary amylase.

CONCLUSIONS: "RESPeRATE™" group showed a decrease in dental anxiety, as evidenced by decreased heart rate. "RESPeRATE™" can be used effectively before dental procedures for anxious children. Salivary alpha amylase was a poor stress biomarker.

The study registration number is NCT04238312, in the ClinicalTrial.gov.

KEYWORDS: Dental anxiety, RESPeRATE™, Salivary Alpha Amylase, Respiratory biofeedback.

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INTRODUCTION

In everyday life, children are often faced with situations that place precise demands on them for adaptation and interaction. A dental visit is an example of such a situation. In some children, this is connected with fear and anxiety (1). Children are more likely to interrupt or refrain their dental appointments due to their elevated dental fear, leading them to encounter an impaired dental health (2). Dental anxiety (DA) is a form of anxiety that occurs when the patient presents to the dentist with the anticipated fear of dental treatment (3). When anxiety up-regulates the sympathetic nervous system (SNS), the pain threshold decreases, and the patient displays physiologic parameters of anxiety, such as increased heart rate (HR). Thus, the down-regulation of the SNS through reduction of pre-procedural anxiety, may definitely lower the pain

reaction to a dental injection (4), which seems to be the major factor of eliciting fear and anxiety (5).

Identifying dentally anxious patients could be achieved through either a semi-structured interview, an anxiety questionnaire, or objective measures (6). Several dental anxiety scales were developed to suit both adults and children (7). The Modified Child Dental Anxiety Scale (MCDAS) is an example of a scale suitable for identifying anxious children. The MCDAS has been used in 8- to 15-year old children. It was shown to have a promising internal consistency and validity (7). It was modified to a version called Faces version of MCDAS (MCDAS_f), to accommodate younger children, and those with restricted cognitive functioning (8).

The autonomic nervous system (ANS) and the respiratory activity exhibit a close association with the experience of emotions. Researchers linked emotions and

anxiety with autonomic, respiratory, and cardiac activities to help analyze the connection between feelings and the physiological parameters (9). An elevation in cardiac output or peripheral resistance will cause increases in blood pressure (10). Therefore, to try to regulate hypertension, relaxation techniques were embraced through biofeedback, meditation in addition to respiratory exercises (11). Meanwhile, heart rate serves as a dependable indicator of children's stress and dental anxiety (12,13).

Biological markers (biomarkers) have a diagnostic or prognostic value and their salivary studies are addressed as "oral-based diagnostics" (14). The two main markers that can be found in saliva are the salivary cortisol, which is conjoined with the hypothalamic-pituitary-adrenal axis and the salivary α -amylase (sAA) that is correlated to the sympathetic nervous system (15). The salivary cortisol does not increase rapidly enough under psychological stressors to provide a good stress index (16). While sAA has been used to assess pain and stress in adolescents and adults undergoing orthodontics (17), and for dental stress assessment in children (18). Various researches have demonstrated that sAA could be an indirect biomarker of sympathetic nervous system activity (19,20).

Psychotherapeutic management of dental anxiety could occur through behavior modification or relaxation techniques (6). Slow and deep breathing has been proved to induce nearly a total inhibition of the sympathetic nervous system (21). Siwaik et al. developed an interactive biofeedback system with audio and visual channels to regulate breathing rate and reduce motion-based artifacts during 4D CT scans (22).

A computerized device known as RESPeRATE™ (InterCure Ltd., New York, USA) is approved by the Food and Drug Administration (FDA), which was revealed to slow the breathing rate, causing dilatation of arterioles and consequently a lowering in the blood pressure (23). A few studies tested its usefulness in anxiety reduction in adults (23,24). Nevertheless, little information is available in literature concerning its use in children. Therefore, this study was conducted to evaluate the effect of RESPeRATE™ on anxiety reduction prior to dental local anesthesia administration in children.

The null hypothesis adopted was that the use of RESPeRATE™ has a similar effect in reducing dental anxiety as compared to that derived by conventional behavior management techniques.

MATERIALS AND METHODS

This randomized controlled trial was performed at the Department of Pediatric Dentistry and Dental Public Health, Alexandria University, Alexandria, Egypt. It proceeded after the approval of the Research Ethics Committee at the Faculty of Dentistry, Alexandria University, Egypt (IRB 00010556)-(IORG 0008839)/6-11-2016. The study is registered with ClinicalTrials.gov, number NCT04238312. The study is written according to Consolidated Standards of Reporting Trials (CONSORT) statement (25). The PICO question was: do children aged 7-12 years (Population: P) using the RESPeRATE™ (Intervention: I), compared to conventional behavior

management techniques (Comparison: C) show reduction in their anxiety levels (Outcome: O)?

Sample size was calculated (<http://powerandsamplesize.com/Calculators/Compare-2-Means/2-Sample-Equality>) using the following assumptions: alpha error= 5%, study power= 80%, mean VAS both in the test and the control groups reported in Morarend et al. (24). The sample size per group was estimated at 55 subjects.

Patients of age range 7 to 12 years were assessed for anxiety using MCDAS_f. After securing the parental consent, those with a score of 19 or more were selected, extremely anxious children scoring above 26 were also included in the study. The MCDAS_f has been translated into Arabic by the first author, then back translated by another bilingual speaker at the Alexandria University to ensure the accuracy of the translation. Experts opinions of Professors of Pediatric Dentistry, Alexandria University, Egypt, were performed for validity of each question. As per their opinions, the question about conscious sedation was removed. A pilot study was done to assess the children's understanding of the questions, and consistency in their answers after one week. The pilot study comprised 20 children, who were not included in the present study. The child pointed to the relevant 'cartoon faces' that represented his/her current feelings or anxiety level. A five-point Likert scale, having a range from 'relaxed/not worried' [1] to 'very worried' [5] was used. A range of 7 (little or no dentally anxious) to 35 (extreme dentally anxious) was calculated to assign the total scores of the MCDAS_f.

From four hundred children screened for eligibility, 110 children were chosen and randomized into two equal groups, each of 55. A total of 290 patients were excluded from the present study because of the refusal of parents to participate in the study, or children had a carbohydrate meal or caffeine-containing beverage within an hour before the procedure. Some children were referred for complex surgery or restorative treatment that required a long treatment session, while few children needed a procedure that did not necessitate the administration of local anesthesia (Figure 1).

One hundred and ten children, randomly divided into two equal groups using the research randomizer (26), participated in this study. The included patients were healthy children (physical conditions ASA I and II) between the ages of 7 and 12 years with MCDAS_f scores of 19 or higher. Those children who needed a dental procedure requiring local anesthesia (LA), after completion of a written parental consent to participate in the study. Children were excluded if they were on anxiolytic medication or affecting cognitive function, and those with special health care needs.

During dental examination, the child was given the MCDAS_f, and if he/she was found eligible, then the selected children were randomly divided into two equal groups each of 55. The child was given a number according to a computer-generated list of random numbers. Allocation was performed by using a block technique, where allocation proportions should be equal. The study was double-blind, the clinical pathologist, and the

statistician were blinded, only the researcher was aware of the allocation group.

Identical methods were performed for both groups. Appointments were scheduled between 10 a.m. and 12 a.m., to avoid any probable diurnal variations of sAA. While each appointment lasted from 15 to 30 minutes according to the treatment needed.

The child was seated in an upright position, after which a finger pulse oximeter (Acc U Rate Pro Series CMS 500DL, Acc U Rate, USA) was placed on his/her index finger of the right hand. A first measurement for HR was documented and the first salivary sample was collected before commencement of the treatment. In the study group, the child was provided a detailed explanation and training of the device used, and then underwent a RESPeRATE™ session for 10 minutes, followed by block or infiltration LA administration (Plain Mepivacaine 3%, 1.8ml, Alexandria Co. for Pharmaceuticals, Egypt). The device trains the user to breathe slowly with extending the expiration time. The child integrates with their guiding tones spontaneously through inhalation and exhalation. Meanwhile, in the control group, Tell, Show and Do technique only was applied prior to LA administration to control patient anxiety. After 5 minutes of LA injection, a second HR measurement was recorded. The second salivary sample was collected 7-10 minutes after dental LA administration.

At least one-hour avoidance of carbohydrates intake, before sample collection, was adopted. Whole saliva was collected twice for the same patient, by unstimulated passive drool. Collecting (about 2mL or more) sAA samples at the same time each day was strictly applied to avoid any diurnal variations and standardization. Within 30 minutes, all samples were refrigerated, and then centrifuged, at 2000xg at 4°C for 10 minutes, within the next 2 hours. All samples were stored at or below -20°C, and analyzed at the Clinical Pathology Department Laboratory, using Alpha Amylase Enzymatic Assay (MAK009, Sigma-Aldrich, Germany). Alpha-amylase (nmole/ml/min) activity was determined using the enzyme kinetic method as per the manufactured instructions, with an overall dilution of 1:500, and absorbance at 405 nanomole (nm).

The Primary outcome measured the proportion of children who were successfully managed by using RESPeRATE™, allowing fulfillment of the required treatment session. While the secondary outcome was assessed through comparing salivary alpha amylase, in a salivary sample, and HR before and after RESPeRATE™ breathing session and through comparing anxiety level reduction between study and control groups.

STATISTICAL ANALYSIS

IBM SPSS for Windows version 23.0 (IBM Corp., Armonk, N.Y., USA) was used for statistical analysis. Significance was set at $P \leq 0.05$. Normality was checked for all variables using descriptive statistics, plots (histogram and boxplots) and Kolmogorov–Smirnov test of normality. Mean and standard deviation (SD) were calculated for all quantitative normally distributed variables. Frequencies and percentages were calculated for dichotomous variables (gender, dental procedure). For quantitative variables, comparing the 2 groups at each

point of time was done using T-test for normally distributed variables (age, modified child dental anxiety scale “MCDAS_f”, heart rate and salivary amylase). Comparing levels before and after LA in the same group was done using paired T-test for normally distributed variables (heart rate and salivary amylase).

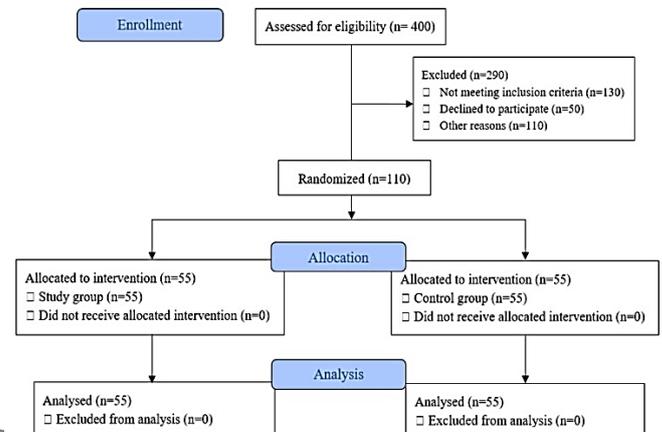


Figure 1: Flow chart of the study

RESULTS

A hundred and ten eligible children were chosen and randomized into two equal groups, each of 55. Children were recruited through a whole year in 2019. Table 1 shows the mean age and MCDAS_f scores for both study and control groups. No significant differences were recorded between the two groups ($P = 0.13, 0.44$ respectively), except for gender which showed significant differences between the two groups ($P = 0.008$).

The heart rate differences in the two groups are shown in table 2 and figure 2. In the study group, a significant decrease in the mean heart rate was detected between values before and after LA administration ($P = 0.001$). Conversely, a significant increase was found in the mean heart rates of the control group, before and after local anesthesia ($P = 0.002$). When comparing heart rates between the study and the control groups, a significant increase was detected in the control group, following administration of LA ($P = 0.01$).

Salivary alpha amylase activity is recorded in table 3 and figure 3. A total of 220 salivary samples were collected from the patients through the study. There were no significant differences found in salivary alpha amylase activity before and after LA ($P = 0.92, 0.48$ respectively), between the two groups. In addition, no significance was found in the mean sAA activity within the same group before and after LA administration ($P = 0.73, 0.35$ respectively).

There was a weak negative non-significant correlation between HR and sAA activity in the study group before and after LA ($P = 0.39, 0.21$ respectively). Meanwhile, in the control group, there was a significant weak positive correlation between HR and sAA activity before LA ($P = 0.048$), whereas a weak negative non-significant correlation was recorded between them after LA ($P = 0.29$).

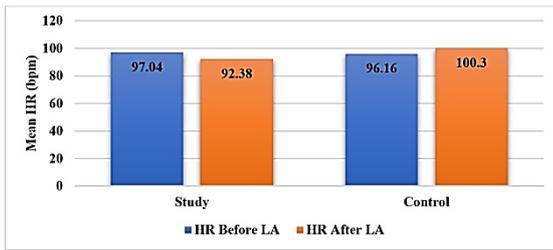


Figure 2: Heart Rate (HR) (bpm) Before and After LA Administration in the 2 Groups.

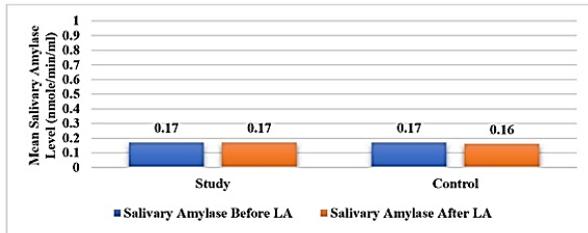


Figure 3: Salivary Alpha Amylase Activity (nmole/min/ml) Before and After LA Administration in the 2 Groups

Table 1: Characteristics of the Study Participants (n=110)

Variable	Study (n=55)	Control (n=55)	Test Value P Value
Age: Mean ± SD ^a	8.84 ± 1.12	8.52 ± 1.09	1.53 0.13
Gender: n (%) ^b			
Males	33 (60%)	19 (34.50%)	7.14 0.008*
Females	22 (40%)	36 (65.50%)	
Baseline MCDAS _f : Mean ± SD ^a	24.15 ± 3.61	23.26 ± 3.25	0.78 0.44

MCDAS_f: Modified Child Dental Anxiety Scale faces version.

*Statistically significant at P ≤ 0.05.

^a Independent Samples T-Test was used.

^b Pearson Chi Square Test was used.

Table 2: Heart Rate (HR) (bpm) Before and After Local Anesthesia (LA) Administration in the 2 Groups

	Study (n=55)	Control (n=55)	T- Test Value P Value
	Mean ± SD		
HR Before LA Administration	97.04 ± 14.90	96.16 ± 19.58	0.26 0.79
HR After LA Administration	92.38 ± 12.57	100.31 ± 19.28	2.55 0.01*
Paired T Test Value P Value (After-Before)	3.47 0.001*	3.24 0.002*	

*Statistically significant at P ≤ 0.05.

Table 3: Salivary Alpha Amylase (sAA) Activity (nmole/min/ml) Before and After LA Administration in the 2 Groups

	Study (n=55)	Control (n=55)	T- Test P Value
	Mean ± SD		
sAA Activity Before LA Administration	0.17 ± 0.05	0.17 ± 0.04	0.10 0.92
sAA Activity After LA Administration	0.17 ± 0.04	0.16 ± 0.04	0.70 0.48
Paired T Test P Value (After-Before)	0.34 0.73	0.95 0.35	

DISCUSSION

Anxiety is a common psychological problem that dentists usually encounter in their dental clinics. Children can mask their fear and anxiety, but the pediatric dentists must be capable of diagnosing and managing the anxious children to avoid behavioral problems and sustain a good relationship. As established from the results of the current study, the null hypothesis was rejected and the use of the RESPeRATE™ device was found to be effective in reducing dental anxiety.

In the current study, 110 anxious children were selected and equally divided randomly into study and control groups. The MCDAS_f was used as a tool for the choice of anxious children aged 7-12 years. This scale was formerly tested for validity and reliability in similar age groups and different populations (27–32). Pediatric patients, in the present study, mostly needed extractions of their primary teeth for orthodontic purposes, in addition to various restorations. In order to assess their anxiety, the Faces version of the MCDAS is thought to be used for young children. Meanwhile, it was found that children, as young as 7 years, would need to be aided with its fulfillment. Dedeepya et al., (33) used the facial image scale for inclusion of anxious children in their study. This scale could be considered as a simpler tool for patient anxiety documentation.

To down-regulate the sympathetic nervous system, a biofeedback device that causes a self-control technique of paced respiration is presented in this study. It was used before the administration of a highly stressful required dental procedure which was LA. A single study session was performed for each patient, where each session included a dental local anesthetic injection to expose the patient to a stressful stimulus. Breathing control using auditory biofeedback was used for self-regulation and relaxation before radiotherapy (22). It was also effective in reducing blood pressure (34), and low back pain (35). Similar to the current study, Morarend et al., (24) concluded in their research that the discomforts related to dental anesthesia were significantly reduced by using the RESPeRATE™ device.

Mostly, all children enjoyed the RESPeRATE™ session. This was indicated by children’s denotations and reactions of enjoying the experience. Some of these include: “I want to have this device at home to relax after a long busy day at school”, “I loved the music and want to repeat the session again” and some children already slept during the session of RESPeRATE™. These comments were found similar to those reported in a study by

Wojcicki et al. who used RESPeRATE™ to help control stress-related diets (34).

The anesthetic drug administered, in the current study, was chosen without a vasoconstrictor to avoid its effect on HR. In addition, HR measurements were recorded on the dental chair in a sitting position to avoid any postural change effects. Results showed that the HR of the study group decreased significantly after LA (Table 2). This ensures that the respiratory biofeedback session was effective. The decrease in HR in the present study, was found in agreement with the findings of Dedeepya et al., (33) when they compared a group receiving biofeedback in their second appointment, with significant reduction in HR. In this context, it was found that the main drawback of the biofeedback devices is that they are found to be not cost-effective, challenging their use in the routine dental visits.

Although, sAA was found to be a less useful indicator of stress in the present study (Table3); the choice of sAA as a biomarker in this study was based on previous research which showed that sAA levels significantly increased by stress (36,37). Researchers suggest that sAA may present over heading readings of short-term stress, unlike salivary cortisol which is considered as an indicator of persistent stress and has a carry-over effect (38). The results of the current study showed that there was a slight change in sAA among both groups in response to the stressful situation of LA administration. However, this was not found significant. A study by AlMaummar et al., (39) concluded that sAA appears to be effective at identifying dental phobia in children although it has weak correlation with anxiety scores. Furlan et al., (13) found a positive correlation between sAA and HR that was amplified by the intensity of dental procedures. However, the present study found a weak negative correlation between the sAA and the HR.

Clinical implication: results of the present study support the findings that dental anxiety can be reduced effectively through using respiratory biofeedback devices and monitoring the human physiological parameters (21,40). Among the limitations of this study, children were not matched by gender. Moreover, the fact that most patients needed extractions, might have affected their behavior and anxiety level. Furthermore, the lack of operator blinding to the use of the study device (RESPeRATE™) was unavoidable. The scarcity of literature addressing children's sAA levels in relation to dental anxiety rendered comparisons perplexing. It is recommended to examine the long-term effect of respiratory biofeedback, in subsequent visits, on children's dental anxiety and it is also recommended to use a larger sample size.

CONCLUSION

Based on the study results, the following conclusions can be derived:

“RESPeRATE™” was effective in the reduction of dental anxiety in children aged 7-12 years.

Heart rate measurement was an excellent significant physiological biomarker for detecting dental anxiety.

Salivary alpha amylase was a non-significant objective indicator of dental anxiety among both groups.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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REFERENCES

- Mendoza-Mendoza A, Perea MB, Yañez-Vico RM, Iglesias-Linares A. Dental fear in children: the role of previous negative dental experiences. *Clin Oral Investig*. 2015;19(3):745–51.
- Armfield JM, Heaton LJ. Management of fear and anxiety in the dental clinic: A review. *Aust Dent J*. 2013;58:390–407.
- Weiner AA. *The Fearful Dental Patient: A Guide to Understanding and Managing*. 1st ed. Boston: Blackwell Publishing Ltd.; 2011. 3–14 p.
- Mustafa O, Parekh S, Ashley P, Anand P. Post-operative pain and anxiety related to dental procedures in children. *Eur J Paediatr Dent*. 2013;14:289–94.
- Paryab M, Hosseinbor M. Dental anxiety and behavioral problems: A study of prevalence and related factors among a group of Iranian children aged 6-12. *J Indian Soc Pedod Prev Dent*. 2013;31:86.
- Appukuttan DP. Strategies to manage patients with dental anxiety and dental phobia: Literature review. *Clin Cosmet Investig Dent*. 2016;8:35–50.
- Al-Namankany A, De Souza M, Ashley P. Evidence-based dentistry: Analysis of dental anxiety scales for children. *Br Dent J*. 2012;212:219–22.
- Howard KE, Freeman R. Reliability and validity of a faces version of the modified child dental anxiety scale. *Int J Paediatr Dent*. 2007;17:281–8.
- Kreibig SD. Autonomic nervous system activity in emotion: A review. *Biol Psychol*. 2010;84:394–421.
- Lilly L, Lee C, Williams G. Hypertension. In: Lilly L, editor. *Pathophysiology of Heart Disease: A Collaborative Project of Medical Students and Faculty*. 5th ed. Philadelphia: Lippincott, Williams, and Wilkins; 2012. p. 301–23.
- Najafian J, Hashemi S. A study of the effect of relaxation and biofeedback-assisted relaxation on patients with mild hypertension. *ARYA Atheroscler*. 2010;1:12–8.
- Mejía-Rubalcava C, Alanís-Tavira J, Mendieta-Zerón H, Sánchez-Pérez L. Changes induced by music therapy to physiologic parameters in patients with dental anxiety. *Complement Ther Clin Pract*. 2015;21:282–6.
- Furlan NFN, Gavião MBD, Barbosa TSTS, Nicolau J, Castelo PMP, Gavião M, et al. Salivary Cortisol, Alpha-Amylase and Heart Rate Variation in Response to Dental Treatment in Children. *J Clin Pediatr Dent*. 2012;37:83–7.
- Thompson LA, Trevathan WR. Cortisol Reactivity, Maternal Sensitivity, and Learning In Three-Month-Old Infants. *Infant Behav Dev*. 2008;31:92–106.

15. Gozansky WS, Lynn J, Laudenslager M, Kohrt W. Salivary cortisol determined by enzyme immunoassay is preferable to serum total cortisol for assessment of dynamic hypothalamic-pituitary-adrenal axis activity. *Clin Endocrinol (Oxf)*. 2005;63:336–41.
16. Bozovic D, Racic M, Ivkovic N. Salivary Cortisol Levels as a Biological Marker of Stress Reaction. *Med Arch*. 2013;67:371–4.
17. Campos MJ da S, Raposo NRB, Ferreira AP, Vitral RWF. Salivary Alpha-Amylase Activity: A Possible Indicator of Pain-Induced Stress in Orthodontic Patients. *Pain Med*. 2011;12:1162–6.
18. Arhakis A, Menexes MG, Coolidge T, Kalfas S. Heart Rate, Salivary α -amylase Activity, and Cooperative Behavior in Previously Naïve Children Receiving Dental Local Anesthesia. *Pediatr Dent*. 2012;34:40–3.
19. Van Stegeren AH, Wolf OT, Kindt M. Salivary alpha amylase and cortisol responses to different stress tasks: Impact of sex. *Int J Psychophysiol*. 2008;69:33–40.
20. De Oliveira VN, Bessa A, Lamounier RPMS, De Santana MG, De Mello MT, Espindola FS. Changes in the salivary biomarkers induced by an effort test. *Int J Sports Med*. 2010;31:377–81.
21. Jerath R, Crawford MW, Barnes VA, Harden K. Self-Regulation of Breathing as a Primary Treatment for Anxiety. *Appl Psychophysiol Biofeedback*. 2015;40:107–15.
22. Siwiak D, Berger J, Yang Y. Catch Your Breath-Musical Biofeedback for Breathing Regulation. In: Audio Engineering Society 127 international convention. 2009.
23. Parati G, Glavina F, Guido O, Alberto M, Paolo C, Benjamin G, et al. P-418 Acute effects of device-guided breathing on cardiovascular parameters and baroreflex sensitivity in normal subjects. *Am J Hypertens*. 2002;15:182A-183A.
24. Morarend QA, Spector ML, Dawson D V, Clark SH, Holmes DC. The Use of a Respiratory Rate Biofeedback Device to Reduce Dental Anxiety: An Exploratory Investigation. *Appl Psychophysiol Biofeedback*. 2011;36:63–70.
25. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *Int J Surg*. 2011;9:672–7.
26. Research Randomizer [Internet]. [cited 2018 Sep 26]. Available from: <https://www.randomizer.org/>
27. Javadinejad S, Farajzadegan Z, Madahain M. Iranian version of a face version of the Modified Child Dental Anxiety Scale: Transcultural adaptation and reliability analysis. *J Res Med Sci*. 2011;16:872–7.
28. Coolidge T, Hillstead MB, Farjo N, Weinstein P, Coldwell SE. Additional psychometric data for the Spanish Modified Dental Anxiety Scale, and psychometric data for a Spanish version of the Revised Dental Beliefs Survey. *BMC Oral Health*. 2010;10. <https://doi.org/10.1186/1472-6831-10-12>
29. Porritt J, Buchanan H, Hall M, Gilchrist F, Marshman Z. Assessing children's dental anxiety: A systematic review of current measures. *Community Dent Oral Epidemiol*. 2013;41:130–42.
30. Zhang H, Xia B, Wang J, Xie P, Huang Q, Ge L. Chinese version of a face version of the modified child dental anxiety scale: transcultural adaptation and evaluation. *Zhonghua kou qiang yi xue za zhi=Zhonghua kouqiang yixue zazhi=Chinese J Stomatol*. 2013;48:403–8.
31. Esa R, Hashim NA, Ayob Y, Yusof ZYM. Psychometric properties of the faces version of the Malay-modified child dental anxiety scale. *BMC Oral Health*. 2015;15. <https://doi.org/10.1186/s12903-015-0013-y>
32. Al-Nasser L, Yunus F, Ahmed A. Validation of Arabic Version of the Modified Dental Anxiety Scale and Assessment of Cut-off Points for High Dental Anxiety in a Saudi Population. *J Int Oral Heal*. 2016;8:21–6.
33. Dedeepya P, Nuvvula S, Kamatham R, Nirmala SVSG. Behavioural and physiological outcomes of biofeedback therapy on dental anxiety of children undergoing restorations: a randomised controlled trial. *Eur Arch Paediatr Dent*. 2014;15:97–103.
34. Wojcicki JM, Geissler JD, Stokes CW, Heyman MB, Tran CT. The Use of the RESPeRATE Device to Lower Blood Pressure in Inner City Obese Adolescents and Children: A Pilot Feasibility Study. *High Blood Press Cardiovasc Prev*. 2013;20:89–92.
35. Kapitza KP, Passie T, Bernateck M, Karst M. First Non-Contingent Respiratory Biofeedback Placebo versus Contingent Biofeedback in Patients with Chronic Low Back Pain: A Randomized, Controlled, Double-Blind Trial. *Appl Psychophysiol Biofeedback*. 2010;35:207–17.
36. Nater UM, Rohleder N, Gaab J, Berger S, Jud A, Kirschbaum C, et al. Human salivary alpha-amylase reactivity in a psychosocial stress paradigm. *Int J Psychophysiol*. 2005;55:333–42.
37. Nater U, Rohleder N. Salivary alpha-amylase as a non-invasive biomarker for the sympathetic nervous system: Current state of research. *Psychoneuroendocrinology*. 2009;34:486–96.
38. Rashkova MR, Ribagin LS, Toneva NG. Correlation between salivary α -amylase and stress-related anxiety. *Folia Med (Plovdiv)*. 2012;54:46–51.
39. Almaummar M, Althabit HO, Pani S. The impact of dental treatment and age on salivary cortisol and alpha-amylase levels of patients with varying degrees of dental anxiety. *BMC Oral Health*. 2019;19:1–8.
40. Rosaura Polak A, Witteveen AB, Denys D, Olf M. Breathing Biofeedback as an Adjunct to Exposure in Cognitive Behavioral Therapy Hastens the Reduction of PTSD Symptoms: A Pilot Study. *Appl Psychophysiol Biofeedback*. 2015;40:25–31.